Rev. Nutr. Vol. 14, 99-129), etc. The transcriptional regulation by these factors are closely involved in the gene expression related to fat cells. It has been reported that the promoter regions of fat cell-related genes including UCP-2 gene contain the binding sequences for these transcriptional regulatory factors (regulator sequences). These sequences in promoters are considered to play important roles in the actual regulation of UCP-2 transcription in vivo.

Accordingly, substances that enhance expression of UCP-2 or UCP-3 gene and protein may be used as antiobestic drugs that reduce body fat content. UCP-2 is also considered to be the major cause of fever in immunological inflammation observed in infection, and substances that inhibit UCP-2 gene activity may reduce fever in immunological inflammation.

If a cell line expressing an appropriate reporter gene connected to the promoter region described above is established, the cell line may be used for screening a drug that promotes or inhibits the UCP-2 expression. In screening substances that may be used as antiobestic drugs, responses more similar to those in vivo can be obtained by including these regulator sequences in the promoter-reporter system, which is very advantageous in screening human antiobestic drugs.

However, human UCP-2 promoter containing the regulator sequence has not yet been identified, and no simple screening method using the promoter described above has been available for substances that affect the human UCP-2 gene expression.

DISCLOSURE OF THE INVENTION

The inventors performed extensive studies, and successfully obtained the human genomic UCP-2 gene using human UCP-2 cDNA fragments as probes in attempt

to establish a screening method for searching substances that affect the human UCP-2 gene expression. The gene was digested with restriction enzymes, and 6.5 kb DNA of the upstream region containing a part of the structural gene encoding UCP-2 was obtained. From the DNA obtained, 3.5 kb DNA containing the base sequence deduced to be the 1st and 2nd exons (2.5 kb DNA as the 5' upstream region) were re-cloned in plasmid DNA.

A plasmid DNA was constructed by connecting luciferase gene as a reporter gene to downstream of the 3.5 kb DNA. Measuring the luciferase activity in transformants of HepG2 cells and MG-63 cells differentiated to fat cell-like cells, UCP-2 promoter was found in the 3.3 kb DNA of the upstream region of the UCP-2 structural gene. As a result of detailed analysis, the regulator sequence that may control the expression of UCP-2 was found.

The inventors proceeded the study based on these findings, and completed the present invention. The present invention relates to the followings:

(1) A DNA containing uncoupling protein-2 (UCP-2)promoter region containing the regulator sequence;

(2) A DNA described in (1) wherein the regulator sequence is a sequence containing peroxisome proliferator response element (PPRE);

(3) A DNA described in (1) wherein the regulator sequence is a sequence containing CCAAT/enhancer binding protein (C/EBP) binding sequence;

(4) A DNA described in (1) wherein the promoter region is a base sequence presented by position 1 to 2270 of SEQ ID NO: 1 or a base sequence containing a part of the said base sequence;

(5) A recombinant vector containing a DNA described in (1);

(6) A recombinant vector described in (5) containing a

DNA having a structural gene under control of UCP-2 promoter region containing a regulator sequence;

(7) A transformant transformed by a recombinant vector described in (5);

(8) A method for screening a compound or its salt that promotes or inhibits UCP-2 promoter activity characterized by use of a transformant described in (7);

(9) A method for screening a compound or its salt that promotes or inhibits heat production characterized by use of a transformant described in (7);

(10) A method for screening an antiobestic drug, an antidiabetic drug, a depressor, an antihyperlipemic drug, and an antipyretic drug characterized by use of a transformant described in (7);

(11) A kit for screening a compound or its salt that promotes or inhibits UCP-2 promoter activity characterized by use of a transformant described in (7);

(12) A compound or its salt that promotes or inhibits UCP-2 promoter activity obtained using a screening method described in (8) or a screening kit described in (11);

(13) A compound or its salt that promotes or inhibits heat production obtained using a screening method described in (9); and

(14) A pharmaceutical composition cntaining a compound or its salt that promotes or inhibits UCP-2 promoter activity obtained using a screening method described in (8) or a screening kit described in (11).

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the base sequence of cDNA containing the human UCP-2 promoter region cloned in Example 1 (continued to Figure 2).